| A                      | PTO-1449   |                              |                    | ATTORNEY'S DKT NO.<br>7953.0004,999 |                 | APPLICATION NO.  |                                       |  |
|------------------------|--|------------------------------|--------------------|-------------------------------------|-----------------|--|---------------------------------------|--|
| NOV 1 6 1998           |  |                              |                    |                                     |                 | the state of the s | 08/844,336                            |  |
|                        | E)   |                              |                    | APPLICANT: Pamela R. Contag, et al. |                 |  |                                       |  |
| PADEMA!                |  |                              |                    | FILING DATE: April 18, 1997         |                 | GROUP: 1641  |                                       |  |
| Carle March            |  |                              | JS PATENT DO       | CUMENTS:                            |                 |  |                                       |  |
| EXAMINER'S<br>INITIALS | PATENT NO.   | DATE                         | N                  | AME                                 | CLASS           | SUBCLASS   | FILING<br>DATE                        |  |
| VR                     | 5,348,867  | 09/20/94                     | Georgiou, et al.   |                                     | 43.5            | 69.7   | 11/15/91                              |  |
| VR                     | 5,591,604  | 01/07/97                     | Fuchs, et al.      |                                     | 425             |  | 07/06/92                              |  |
|                        |  | FOR                          | EIGN PATENT!       | OOCUMENTS *                         |                 | 3/1/1/19   |                                       |  |
| EXAMINER'S<br>INITIALS | PATENT NO.   | DATE                         | COUNTRY            |                                     | CLASS           | SUBCLASS   | Translation                           |  |
| VR                     | WO 97/08553  | 6 Mar 1997                   | PCT                |                                     |                 |  |                                       |  |
|                        | OTHER D  | OCUMENTS'                    | Including Antho    | "Title" Data" pa                    |                 |  | Oliman Grand and and                  |  |
| VR                     | Collet, T.A., et al. 1<br>Acad. Sci. USA 89:1  | 1992 "A binary<br>0026-10030 | plasmid system f   | or shuffling comb                   | oinatorial anti | body libraries.  | " Proc. Natl.                         |  |
| 41/                    | Francisco, J.A., et al. 1994 "The Expression of Recombinant Proteins on the External Surface of Escherichia coli." Ann. N.Y. Acad. Sci. 745:372-382  |                              |                    |                                     |                 |  |                                       |  |
| VR                     | Fuchs, et al. 1991 "Targeting Recombinant Antibodies to the Surface of Escherichia Coli: Fusion to a Peptidoglycan Associated Lipoprotein. Bio/Technology 9:1369-1372                                    |                              |                    |                                     |                 |  |                                       |  |
| VR                     | Georgiou, G., et al. 1993 "Practical applications of engineering Gram-negative bacterial cell surfaces."  TIBTECH 11:6-10  |                              |                    |                                     |                 |  |                                       |  |
| - 1                    | Georgiou, G., et al. 1997 "Display of heterologous proteins on the surface of microorganisms: From the screening of combinatorial libraries to live recombinant vaccines." Nature Biotechnology 15:29-34 |                              |                    |                                     |                 |  |                                       |  |
| VR                     | Little, M., et al. 1993 "Bacterial surface presentation of proteins and peptides: an alternative to phage technology?" TIBTECH 11:3-5  |                              |                    |                                     |                 |  |                                       |  |
| VR<br>VR               | Little, M., et al. 199   | 5 "Human ant                 | ibody libraries in | Escherichia coli."                  | ournal of Biote | chnolou 41:187   | -195                                  |  |
| UR_                    | Stahl, S., et al. 1997   | "Bacterial sur               | ace display:trend  | s and progress."                    | TIBTECH 15      | 185-192  |                                       |  |
|                        | <u> </u>   |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  | <del></del>                           |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  | · · · · · · · · · · · · · · · · · · · |  |
|                        |  |                              | <del> </del>       |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 |  |                                       |  |
|                        |  |                              |                    |                                     |                 | 0  |                                       |  |
|                        |  |                              |                    |                                     |                 | · · · · · · · · · · · · · · · · · · ·  |                                       |  |
| XAMINER                | V.Ra   |                              | DATI               | CONSIDERED                          | 11-             |  |                                       |  |
|                        | 4.16   |                              |                    |                                     | 1/99            |  |                                       |  |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.





|                                 | <u> </u>  |                |                            | T                      |             | LA DRIVIGATION A | Io.            |  |  |
|---------------------------------|---|----------------|----------------------------|------------------------|-------------|------------------|----------------|--|--|
| INFORMATION DISCLESURE CITATION |   |                |                            | ATTORNEY'S DKT NO      |             | APPLICATION NO.  |                |  |  |
| FORTH 149                       |   |                |                            | 7953.0004.9            |             | 08/844,336       |                |  |  |
|                                 |   |                |                            | APPLICANT: Pamel       | a R. Contag | g, et al.        |                |  |  |
|                                 |   |                |                            | FILING DATE: April     | 18, 1997    | GROUP: 1641      |                |  |  |
| <u> </u>                        |   | U              | S. PATENT DO               | CUMENTS                |             |                  |                |  |  |
| EXAMINER'S<br>INITIALS          | PATENT NO. DATE NAME  |                |                            |                        | CLASS       | SUBCLASS         | FILING<br>DATE |  |  |
| VR                              | 5,650,135   | 07/22/97       | contag, craii 127 1,1      |                        |             |                  | 07/01/94       |  |  |
|                                 |   | FOR            | EIGN PATENT                | DOCUMENTS              |             |                  |                |  |  |
| EXAMINER'S<br>INITIALS          | PATENT NO.  | DATE           | ATE COUNTRY CLASS SUBCLASS |                        |             | Translation      |                |  |  |
|                                 | OTHER D   | OCUMENTS (     | Including Auth             | or, Title, Date, Perti | nent Pages  | , Etc.)          |                |  |  |
| 10                              | Blom, et al., 1993 ".   | A Baculovirus- | Expressed Fusion           | n Protein Containing   | the Antibo  | ody-Binding Do   | omain of       |  |  |
| VR.                             | Protein A and Insect Luciferase." BioTechniques 14(5):800-809   |                |                            |                        |             |                  |                |  |  |
|                                 | Brennan, et al., 1995 "A Molecular Sensor System Based On Genetically Engineered Alkaline Phosphatase."   |                |                            |                        |             |                  |                |  |  |
| YR                              | Proc. Natl. Acad. Sci. USA 92:5783-5787   |                |                            |                        |             |                  |                |  |  |
| ir                              | Borrebaeck et al., 1992 "Kinetic analysis of Recombinant Antibody-Antigen Interactions: Relation Between Structural Domains and Antigen Binding." <i>Biotechnology</i> <b>10(6)</b> :697-698  |                |                            |                        |             |                  |                |  |  |
| VR                              | Brasier, et al 1992 "Luciferase Reporter Gene Assay in Mammalian Cells." <i>Methods. in Enzymology</i> 216:386-396.   |                |                            |                        |             |                  |                |  |  |
| VP                              | Candido, et al., 1996 "Transgenic Caenorhabditis elegans strains as biosensors." Trends in Biotechnology 14:125-  |                |                            |                        |             |                  |                |  |  |
| VR                              | Contag, et al., 1997 "Visualizing Gene Expression in Living Mammals Using a Bioluminescent Reporter."  Photochemistry and Photobiology 66(4):523-531  |                |                            |                        |             |                  |                |  |  |
| VR                              | Contag, et al., 1995 "Photonic detection of bacterial pathogens in living hosts." <i>Molecular Microbiol ogy</i> 18(4):593-603  |                |                            |                        |             |                  |                |  |  |
| VR                              | DiLella, et al., 1988 "Utility of firefly luciferase as a reporter gene for promoter activity in transgenic mice."  Nucleic Acids Research 16(9):4159   |                |                            |                        |             |                  |                |  |  |
| VR                              | Enberg, B., et al. 1994 "Growth hormone (GM) regulation of a rat serine protease inhibitor fusion gene in cells transfected with GH receptor cDNA." Journal of Molecular Endocrinology 12:39-46   |                |                            |                        |             |                  |                |  |  |
| VR                              | Frackman, et al., 1990 "Cloning, Organization, and Expression of the Bioluminescence Genes of Xenorhabdus Juminescens." Journal of Bacteriology 172(10):5767-5773.  |                |                            |                        |             |                  |                |  |  |
| VF                              | Griffiths et al., 1998 "Strategies for selection of antibodies by phage display." Current Opinion in Biotechnology 9:102-108.   |                |                            |                        |             |                  |                |  |  |
| 1P                              | Hannibal, et al. 1994 "Multiple <i>cis</i> -acting elements in the human immunodeficiancy virus type 2 enhancer mediate the response to T-cell receptor stimulation by antigetn ina T-cell hybridoma line." <i>Blood</i> 83(7):18391846 |                |                            |                        |             |                  |                |  |  |
| VR                              | Hasemann, et al., 1989 "Immunoglobulins: Structure and Function", In Fundamental Immunology 2nd (Ed.) W.E. Paul:209-233.  |                |                            |                        |             |                  |                |  |  |
| JR.                             | Hoogenboom, et al., 1991 "Multi-subunit proteins on the surface of filamentous phage: methodologies for displaying antibody (Fab) heavy and light chains." <i>Nucleic Acids Research</i> 19(15):4133-4137                               |                |                            |                        |             |                  |                |  |  |
| IR                              | Hooper et al., 1994 "Low-Light Imaging Technology in the Life Sciences." Journal of Bioluminescence and Chemiluminescence 9:113-122.  |                |                            |                        |             |                  |                |  |  |
| NP                              | Huse et al., 1989 "Generation of a Large Combinatorial Library of the Immunoglobulin Repertorie in Phage Lambda." Science 246:1275- 1281  |                |                            |                        |             |                  |                |  |  |
| VR                              | Israel, et al., 1991 "Bioluminescence assay for gene expression by continuously growing mammalian cells: application for detection of human immunodeficiency virus type 1 (HIV-1)." Gene 104:139-145.                                   |                |                            |                        |             |                  |                |  |  |
| VIR                             | Karube, et al., 1994, "Immobilized cells used for detection and analysis" Curr. Opin. Biotechnol. 5(1):54-59.   |                |                            |                        |             |                  |                |  |  |
| 1                               | Kasahara, et al., 1991 "Molecular analysis of the Salmonella typhimurium phoN gene, which encodes nonspecific acid phosphatase." Journal of Bacteriology 173(2):6760-6765   |                |                            |                        |             |                  |                |  |  |

|          | OF DEMARKET  |  |  |  |  |  |
|----------|--|--|--|--|--|--|
| VR       | Kasahara, et al., 1992 "Molecular analysis of the Esherichia coli phoP-phoQ operon. "Journal of Bacteriology 174(2):492-498.   |  |  |  |  |  |
| VR       | Kohl et al., 1990, "Engineered gene for Escherichia coli alkaline phosphatase for the construction of translational fusions." Nucleic Acids Res. 18:1069   |  |  |  |  |  |
| VR       |  |  |  |  |  |  |
| VR       | Kovacs, et al., 1991 "Firefly luciferase as a marker for herpesvirus (pseudorabies virus) replication in vitro and in vivo" J. Gen. Virol. 72:2999-3008  |  |  |  |  |  |
| VR       | McCafferty, et al., 1990 "Phage antibodies: filamentous phage displaying antibody variable domains." <i>Nature</i> 348:552-554   |  |  |  |  |  |
| NR       | Miller, et al., 1989 "A two-component regulatory system (phoP phoQ) controls Salmonella typhimurium virulence." <i>Proc. Natl. Acad. Sci. USA</i> 86:5054-5058.  |  |  |  |  |  |
| VR       | Miller, S.I., 1991 "PhoP/PhoQ: macrophage-specific modulators of Salmonella virulence?" Molecular Microbiology 5(9):2073-2076  |  |  |  |  |  |
| VR       | Mueller-Klieser, et al., 1993 "Geographical Mapping of Metabolites in biological tissue with quantitative bioluminescence and single photon imaging." Institute of Physiology & Pathophysiology 16 November 1992 and in revised from 23 January 1993   |  |  |  |  |  |
| VR       | Orum, et al., 1993 "Efficient method for constructing comprehensive murine Fab antibody libraries displayed on phage." Nucleic Acids Res 21:4491-4498.   |  |  |  |  |  |
| VR       | Ottemann, et al., 1993 "Converting a transmembrane receptor to a soluble receptor: recognition domain to effector domain signaling after excision of the transmembrane domain." <i>Proc. Natl. Acad. Sci. USA</i> 94:11201-11204   |  |  |  |  |  |
| JP       | Parkinson, J.S., 1993 "Signal Transduction Schemes of Bacteria." Cell 73:857-871.  |  |  |  |  |  |
| VR       | Ramanathan, et al., 1997 "Bacterial biosensors for monitoring toxic metals." Trends Biotechnol 15:500-506  |  |  |  |  |  |
| VR       | Ronald et al., 1990, "Construction of broad-host-range for the selection of divergent promoters." Gene 90:145-   |  |  |  |  |  |
| NF       | Rupani, et al., 1996 "Characterization of the Stress Response of a Bioluminescent Biological Sensor in Batch and Continuous Cultures." <i>Biotechnol. Prog.</i> 12:387-392.  |  |  |  |  |  |
| VR       | Soncini, et al., 1995 "Transcriptional autoregulation of the Salmonella typhimurium phoPQ operon." Journal of Bacteriology 177(15):4364-4371   |  |  |  |  |  |
| VR       | 1 Decided to the control of the cont |  |  |  |  |  |
| VR.      | Swift, et al., 1994 "Gram-negative bacterial communication by <i>N-acyl</i> homoserine lactones: a universal language?." <i>Trends in Microbiology</i> 193:2(6):193-198  |  |  |  |  |  |
| VR       | Szittner, et al., 1990 "Nucleotide Sequence, Expression, and Properties of Luciferase Coded by lux genes from a Terrestrail Bacterium." J. Biol. Chem. 265:16581-16587   |  |  |  |  |  |
| · VR     | Van Dyk, et. al. 1994 "Rapid and sensitive pollutant detection by induction of heat shock gene-bioluminescen gene fusion's." Applied and Environmental Microbiology 60(5):1414-1420  |  |  |  |  |  |
| VR       | Weiss, et al., 1994 "Application of an alkaline phosphatase fusion protein system suitable for efficient screening and production of Fab-enzyme conjugates in Escherichia coli" J. Biotechnol. 33:43-53  |  |  |  |  |  |
| VR       | Vescovi, et al., 1996 "Mg2+ as an Extracellular signal: environmental regulation of Salmonella virulence." <i>Cell</i> 84:165-174.   |  |  |  |  |  |
| VR       | Willardson, et al., 1998 "Development and Testing of a Bacterial Biosensor for Toluene-Based Environmental Contaminants." <i>Applied and Environmental Microbiol ogy</i> 64(3):1006-1012   |  |  |  |  |  |
| N/C      | Wood, et al., 1996 "Transduction in microbial biosensors using multiplexed bioluminescene." Biosensors & Bioelectronics Vol. 11(3):207-214   |  |  |  |  |  |
|          | Xi et al., 1991, "Cloning and Nucleotide Sequences of lux Genes and Characterization of Luciferase of Xenorhabdus luminescens from a Human Wound." J. Bact. 173:1399-1405.   |  |  |  |  |  |
| EXAMINER | DATE CONSIDERED 1/99   |  |  |  |  |  |
|          |  |  |  |  |  |  |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.